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**Enhancing Warfighter Cognitive Abilities
with Transcranial Magnetic Stimulation:
a Feasibility Analysis**

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Summary

This study examined the feasibility of using transcranial magnetic stimulation (TMS) to enhance warfighter cognitive abilities. An extensive literature review was conducted and several TMS laboratories were visited. Discussions were also held with several of the leading experts in the field of brain stimulation. The final recommendation of this study is to pursue TMS research with prudence, as the current state of the technology is still very oriented towards basic science exploration. Several studies have begun to show cognitive enhancement benefits of TMS in basic tasks, but work has yet to be done in more complex domains that would be of greatest benefit to the warfighter. However, with the possible advantages to be gained through this and similar technologies, the Air Force Research Laboratory should begin researching ways to improve current application techniques while incorporating more operationally-derived performance tasks.

1. Introduction

As our military evolves into a more net-centric force, with larger and larger amounts of information being piped to the warfighter, it becomes vital that human operators are able to wisely discriminate between and integrate many different pieces of information to make rapid, well-informed decisions. Although technology capabilities continue to increase, the actual human being making the decisions has remained basically the same. Soldiers must eat, sleep, discriminate between friend and foe, heal when wounded, and George Miller's (1956) mantra of " 7 ± 2 " – the number of items that can be retained in immediate memory – still pertains. The allure of artificial enhancement is great, especially when the gains to be made are so immense. For instance, research may yield ways to enhance individuals to become fatigue-resistant or even less fearful.

According to the Joint Human Performance Enhancement (JHPE) Joint Capabilities Document (2006), some identified capabilities needed to achieve future military objectives include "Enhance Warfighter Sensory, Cognitive, and Motor Capabilities" and "Enhance Warfighter Learning, Communications, and Decision-Making". More specifically, these consist of "Enhance recognition of sensory stimuli beyond unaided levels" and "Cognitive abilities increased above baseline levels to enhance speed and accuracy of decision-making". Through cognitive enhancement techniques and technologies, the operators' mental abilities may be expanded and become less of a limiting factor.

Enhancement of cognitive abilities is a part of the much larger domain of human performance optimization (HPO). In a broad sense, HPO is the "relatively precise, controlled and combined application of certain substances and devices over the short and long-term to achieve optimization in a person or unit's performance *overall*" (Russell, Bulkley, & Grafton, 2005). While it is unlikely a single discovery will yield the advantage of HPO, performance enhancement substances and devices as well as the expertise in applying those discoveries in order to best optimize military human performance are vital to attain this advantage.

In particular, this study examines the feasibility of enhancement of a soldier's cognitive abilities through the use of transcranial magnetic stimulation (TMS). As Russell and colleagues (2005) state in their HPO final report, "Ampakines, calcineurin inhibitors, orexins, salvia lavandulaefolia, and TMS are all short-term and relatively feasible developments that can be applied to produce a sum effect of optimized learning and recall." Later in the report, TMS is suggested as being a possible "cognition optimizer" and possibly able to "increase focus and concentration" leading to optimized learning, acuity, and memory. While cognitive enhancement with TMS is the main focus of this study, other possible methods to be used, perhaps in conjunction with TMS, are also discussed briefly.

2. Definitions

As with any report, it is important to ensure a standard definition for the words being used. For purposes of this report, the terms below are assumed to convey the following concepts:

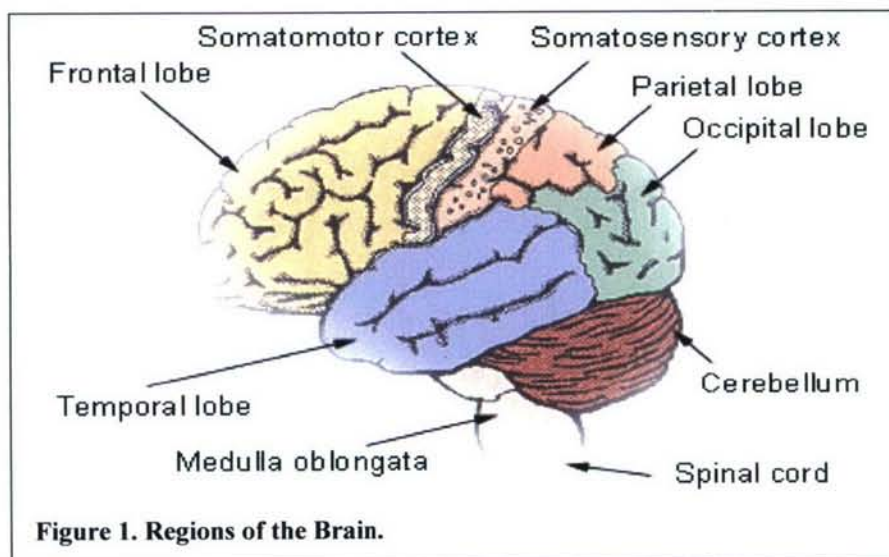
2.1 Cognition – an information processing view of an individual's psychological functions such as memory, attention, perception, action, problem-solving, mental imagery, and emotion

2.2 Enhancement – temporary or permanent attempt to overcome limitations of the human body; this may be increasing abilities beyond normal levels or augmenting deficient abilities (such as when in a fatigued state)

2.3 Savant Syndrome – a person having extraordinary mental abilities not found in most people; often, this phenomenon is found in autistic individuals having both severe developmental or mental handicap and extraordinary mental abilities – however, this is *not always* the case; savant syndrome skills involve amazing feats of memory and may also include unusual abilities in arithmetic calculation, art, or music

3. Brain Basics

Weighing around three pounds and consuming about a quarter of the body's energy, the brain is immense and complex. It controls the central nervous system, the peripheral nervous system, and regulates virtually all human activity. The brain is also the source of the conscious, cognitive mind, which is a set of processes related to perception, interpretation, imagination, memories, and language. Divided into two hemispheres, the structures of the brain are replicated on each side. Regions of each hemisphere of the brain are often divided up accordingly:



3.1 Regions

Frontal lobe – This region of the brain is largely responsible for many executive functions and has been found to play a part in impulse control, judgment, language production, working memory, motor function, problem-solving, sexual behavior, socialization, and spontaneity. Further, the frontal lobe has been shown to assist in planning, coordinating, controlling, and executing behavior. The primary motor cortex (somatomotor cortex)

works in association with the pre-motor areas of the frontal lobe to plan and execute movements.

Parietal lobe – Positioned above the occipital lobe and behind the frontal lobe, the parietal lobe is responsible for integration of sensory information from different modalities, particularly when determining the spatial location of objects. The parietal lobe also plays important roles in the manipulation of objects. Also found in this lobe is the somatosensory cortex (primary sensory cortex).

Occipital lobe – Containing most of the anatomical region of the visual cortex, the occipital lobe is the visual processing center of the brain. The first functional area, the primary visual cortex, contains a low-level description of the local orientation, spatial-frequency, and color properties within small receptive fields. From here, the primary visual cortex projects to the occipital areas of the ventral stream (mostly processing object recognition) and the dorsal stream (mostly processing object spatial orientation).

Temporal lobe – If the brain were imagined as boxing gloves, the temporal lobes are where the thumbs would be. This lobe is involved in auditory processing and contains the primary auditory cortex. It is also involved in semantics both in speech and vision (the ventral stream from the visual cortex). Deeper in the temporal lobe is the hippocampus, which therefore ties the temporal lobe to memory formation as well.

Cerebellum – Translated as “little brain”, the cerebellum is a region of the brain that plays an important role in the integration of sensory perception and motor output. Specifically, the cerebellum integrates with the motor cortex and spinocerebellar tract (which provides proprioception) to fine-tune motor movements such as equilibrium, posture, and motor learning. More recent research also suggests the cerebellum’s role in many cognitive functions including attention and the processing of language, music, and other sensory temporal stimuli.

Brain stem (medulla oblongata and part of the spinal cord) – This region of the brain is typically considered as the pons, medulla oblongata, and midbrain. Some of the functions these structures are involved in include sensation, vision, arousal, consciousness, motor function, emotion, alertness, and autonomic reflexes.

3.2 Neural Functioning

Neurons are electrically excitable cells in the nervous system that process and transmit information. They are the core component of the brain, spinal cord, and peripheral nerves (although the role of glia in processing neural information has begun to be appreciated). Typically, neurons are composed of a soma (cell body), a dendritic tree, and an axon. Most neurons receive input on the cell body and dendritic tree and transmit output through the axon. Neurons communicate via chemical and electrical synapses, known as synaptic transmission.

The fundamental process that triggers synaptic transmission is the action potential, a propagating electrical signal that is generated by exploiting the electrically excitable membrane of the neuron. Once an action potential is triggered, a signal is

typically sent down the axon of the neuron to the axon terminal where a neurotransmitter chemical is released, causing communication with other target neurons.

Neurons communicate with one another via synapses, where the axon terminal of one cell impinges upon a dendrite, soma, or (less commonly) an axon. Some neurons can have over 1,000 dendritic branches and make connections with tens of thousands of other cells; other neurons may have only one or two dendrites, each of which receives thousands of synapses. A synapse can be excitatory or inhibitory and will either increase or decrease activity in the target neuron. Some neurons may also communicate through electrical synapses, which are direct, electrically-conductive junctions between cells. The chemical synapse is a chain reaction process that occurs as follows: an action potential reaches the axon terminal; this opens voltage-gated calcium channels in the target neuron, allowing calcium ions to enter the terminal; calcium causes synaptic vesicles filled with neurotransmitter molecules to fuse with the membrane, releasing their contents in the synaptic cleft; and, the neurotransmitters diffuse across the synaptic cleft and activate receptors on the postsynaptic neuron.

When neurons synapse with other neurons, the signal can either strengthen or weaken the connection between the neurons, making it easier or harder for subsequent synapses to create an action potential. Long-term potentiation (LTP) is an increase in the strength of a chemical synapse and can last from minutes to years. Long-term depression (LTD) is the weakening of a neuronal synapse that can last from minutes to years. LTDs can result from either a strong synaptic stimulation to a persistent weak synaptic stimulation.

4. Transcranial Magnetic Stimulation

Noninvasive, focal manipulation of brain function became reality with the advent of transcranial magnetic stimulation (TMS) in the 1980s. TMS is designed on the principle of electromagnetic induction. When an electrical current is passed through a magnetic coil, the resulting magnetic field can penetrate through the skull and into the outer layers of cortical tissue where it induces electrical activity in the targeted neurons.

The exact mechanism of action for TMS is not completely clear, but the prevailing thought is that it works by changing the membrane potential in neurons. Although the magnetic stimulation does not involve direct passage of electric currents through the body, at the cellular level, the mechanisms of stimulation are the same. Charge is moved across an excitable cellular membrane, creating a transmembrane potential or nerve depolarization voltage. When sufficient enough, this voltage can cause membrane depolarization and initiate an action potential, which then propagates along a nerve like any other action potential (George & Belmaker, 2007). Some studies have also suggested that TMS may have neurobiological effects in ways other than just creating action potentials (Ji et al., 1998).

Many studies have demonstrated that TMS is safe as long as the proper guidelines are followed. There have been no significant cognitive (Little et al., 2000; Triggs et al., 1999), neurological (Nahas et al., 2000), or cardiovascular sequelae reported as a result of repetitive TMS (rTMS) (George & Belmaker, 2007). Single-pulse TMS has been in use for nearly 15 years and is regarded as safe and virtually without lasting side effects. Repetitive TMS (rTMS), on the other hand, can produce a range of lasting effects on

cerebral function, some of which are desirable from the clinical point of view, such as momentary disruption of cognitive function (George & Belmaker, 2007). It can also induce epileptic seizures predictably if it is not applied with limits on the stimulation parameters.

Single-pulse means a single pulse or paired pulses are delivered nonrhythmically and not more than once every few seconds. The most common side effect reported has been local discomfort and headache. Guidelines have been developed to minimize the risk of seizures caused by rTMS. In rTMS, pulses are delivered in “trains”, such as 7-seconds of 3-Hz stimulation or 15 minutes of 1-Hz stimulation.

Some of the acute and lasting effects that have been observed depend largely on the dosing protocol (single pulse, repetitive pulse, pulse train, etc.). Acute effects include direct activation of neural circuits (for an overview of some rTMS effects, see Attachment A). Often times, these stimulations may elicit observable responses (e.g., motor twitch), disrupt ongoing processes (e.g., speech arrest), or facilitate ongoing processes (e.g., speed reaction time). Lasting effects include changes in the neuroplasticity of the targeted area. For example, the synaptic efficacy may be changed through LTP or LTD. Other effects include altering neurotropic factors, modulation of cortical excitability, and modulation of functional connectivity (S. H. Lisanby, presentation, 05 March 2007). The general consensus is that low frequencies of rTMS (1 Hz) attenuate, whereas higher frequencies (5-20 Hz), increase blood flow and metabolism. These effects are not only seen locally at the site of rTMS, but also, in some instances, in a widespread downstream fashion as well (George & Belmaker, 2007).

Researchers in London reviewed the effects of single and repetitive TMS delivered to the primary motor and premotor areas and measured across distributed brain regions using electrophysiological measures (e.g. motor thresholds, motor evoked potentials, and paired-pulse stimulation), functional neuroimaging (EEG, PET, and fMRI), and behavioral measures (Lee, Siebner, & Bestmann, 2006). The study revealed trains of rTMS have lasting effects on the excitability of intrinsic and corticofugal neurons, altering the responsiveness of local and remote sites. These effects lead to distributed changes in synaptic activity at rest and during a range of motor tasks. Further, the researchers demonstrated it is possible to impair or improve performance following rTMS, but for most simple motor tasks performance is unaltered. The researchers propose a possible explanation for this effect: changes in distributed activity observed with functional imaging during motor behavior may represent compensatory activity, enabling maintenance of performance; stimulation of additional cortical areas appears to impair performance.

The clinical applications of TMS is a large area of research, with major thrusts focusing on the treatment of depression, anxiety disorders, and epilepsy. However, several other possible applications are also being considered. For example, some researchers have suggested TMS may be useful in improving hemispatial neglect in clinical patients (Fierro, Brighnia, & Bisiach, 2006). Another study demonstrated that two weeks of daily repetitive TMS over the left or right temporoparietal cortex reduces symptoms in patients with schizophrenia who suffer from treatment-refractory auditory hallucinations (Lee et al., 2004).

While it is clear that TMS may have numerous applications in the clinical environment, recent evidence also suggests that the usefulness of TMS may extend

beyond the clinical and basic research realms. Besides reducing effects of disease or augmenting deficient cognitive abilities, TMS has been shown to enhance cognitive capabilities in normal individuals.

5. Enhancing Cognitive Functioning with TMS

In its initial applications, TMS was used for disruption of brain activity during ongoing processes to better understand how the brain worked. However, recent research suggests TMS may have the ability to potentiate cognitive abilities, possibly by modulating local synaptic activity, disrupting networks that interfere with task performance, and/or modulation of brain oscillatory activity.

5.1 Past Research

Many studies have demonstrated the ability of TMS to enhance cognitive abilities; however, the intent of the study is typically to better understand a region of the brain for the treatment of a disease, not to create a cognitive enhancement technique for normal individuals. Because of this, the improvements seen in performance are rarely followed up with subsequent research attempting to fine-tune the potentiation.

A series of studies by German researchers found facilitatory effects of single-pulse and repetitive TMS on a simple picture naming task (Mottaghy, Sparing, & Topper, 2006). One study revealed significant shortening of picture naming latencies after single-pulse TMS over Wernicke's area; however, accuracy of the response was not affected by this speed effect and TMS over the dominant motor cortex or over the non-dominant temporal lobe showed no facilitation of picture naming. A subsequent study examined the effects of rTMS on picture naming facilitation, observing rTMS facilitation only over Wernicke's area and no effect over the visual cortex, Broca's area, or over the corresponding sites in the non-dominant hemisphere. Mottaghy and colleagues proposed single-pulse TMS is able to facilitate lexical processes due to a general preactivation of language-related neuronal networks when delivered over Wernicke's area and rTMS over Wernicke's area may lead to facilitation by shortening the linguistic processing time.

Researchers at Stanford demonstrated enhancement of phonological memory following TMS (Kirschen et al., 2006). Based on the premise that phonologically similar items (i.e., "mell, rell, gell) are more difficult to remember than dissimilar items (i.e., "shen, floy, stap"), Kirschen and colleagues applied low-frequency TMS, guided by functional magnetic resonance imaging (fMRI), to the left inferior parietal (LIP) lobule. With this stimulation the researchers attempted to disrupt the mutual interference of the phonologically similar items in the phonological store. The results of the study were consistent with the behavioral performance of patients with certain neurological damage (e.g., paradoxical functional facilitation); memory for phonologically similar, but not dissimilar, items was enhanced following TMS relative to placebo and control region stimulations.

At the National Institute of Neurological Disorders and Stroke, a part of the National Institutes of Health, researchers utilized rTMS on 16 normal volunteers to investigate the role of the left dorsolateral prefrontal cortex in analogical reasoning (Boroojerdi, 2001). rTMS over the left and right prefrontal cortex, over the left motor cortex, and sham stimulation over the left prefrontal cortex were administered during

memory and analogic reasoning conditions. Results indicated that rTMS applied to the prefrontal cortex led to a significant reduction in response times only in the analogy condition without affecting accuracy.

Facilitation of performance in memory has been studied by several groups. For example, Kohler and colleagues (2004) performed a study which suggests rTMS may enhance episodic memory when applied to the left inferior prefrontal cortex. Working memory was shown to be enhanced with rTMS of the precuneus by researchers at Columbia University (Luber et al., 2006). Using a delayed match-to-sample task, the investigators applied rTMS at 1-, 5- or 20-Hz to either the left dorsolateral prefrontal or midline parietal cortex during the retention (delay) phase of the task. Only 5-Hz stimulation to the parietal site resulted in significant decrease in reaction time without a corresponding decrease in accuracy. This finding was replicated in a subsequent study in which 5-Hz rTMS at the parietal site was applied during the retention phase or during presentation of the recognition probe. The results showed significant speeding of reaction time in the retention phase but not the probe phase. The authors conclude that TMS may improve working memory performance in a manner that is specific to the timing of stimulation relative to performance of the task and to the stimulation frequency.

More recently, Luber and colleagues incorporated a sleep deprivation component to their TMS research (article has recently been submitted to journal). Based on their previous research demonstrating the right combination of rTMS timing, frequency, and site of application can facilitate performance, the researchers set out to reverse working memory deficits caused by sleep deprivation. Guiding the TMS application according to an fMRI network associated with resilience to sleep deprivation-induced performance impairments, Luber and colleagues applied rTMS to the upper occipital site, resulting in a reduction of the sleep-induced reaction time deficit without a corresponding decrease in accuracy. Stimulation to other sites did not show this effect. The degree to which the performance was enhanced correlated with the degree to which each individual failed to sustain activation of the fMRI network. rTMS was later applied to the same subjects after recovery from sleep deprivation and no effects were found.

While studying the brain mechanisms responsible for allowing visual stimulus to enter our conscious awareness, researchers in Canada applied single pulse TMS to the frontal eye field (an area known to control eye movements) (Grosbras & Paus, 2003). Volunteers participated in a backward masking task in which they were able to detect a target in a small proportion of trials. It was found that a single pulse of TMS over the frontal eye field shortly before the target's onset facilitated visual sensitivity; subjects were able to detect an otherwise subliminal object. These results demonstrated that modulating the neuronal activity of the frontal eye field can enhance visual detection.

Other TMS research has used the stimulation as a form of electrical interference. Pulses are delivered to momentarily disrupt normal synaptic transmission. With this method, researchers can test hypotheses about the function of brain regions, helping to establish the causal role of a cortical region for a given behavior. But this use of TMS has rarely, if ever, led to an enhancement of cognitive functioning in normal individuals. Typical enhancement is seen by priming a region of the brain just before task performance, and may also be possible by temporarily inhibiting specific regions of the brain for extended periods of time, leading to paradoxical functional facilitation (PFF).

5.2 Preactivation and Inhibition

The main theory as to the mechanism by which TMS enables enhanced cognitive abilities is through neuronal preactivation or priming. According to this theory, stimulating an area of the brain pre-activates neurons in that region, increasing their propensity to fire. This theory is supported with the functional imaging evidence suggesting TMS applied to an area leads to an increase in regional blood flow and metabolism (George & Belmaker, 2007). Enhanced cortical excitability can be achieved with single or repetitive pulse TMS. With single pulse TMS, it is possible to momentarily interfere with the functioning of a region or enhance excitability in a region for a very short amount of time (less than 500 ms); however, these stimulations may have longer lasting effects on more distant cortical regions reached by trans-synaptic cortico-cortical effects (Pascual-Leone, Walsh, & Rothwell, 2000).

While it may be argued that single pulse TMS causes a “temporary lesion” by transiently disrupting functioning, rTMS allows researchers the ability to create longer lasting effects. rTMS can be used to continually excite an area or, with the appropriate frequency and intensity, create a longer lasting “virtual lesion”. For example, some researchers have suggested that 15 minutes of 1-Hz rTMS can temporarily inhibit a region of the brain for up to 45 minutes (Snyder et al., 2003).

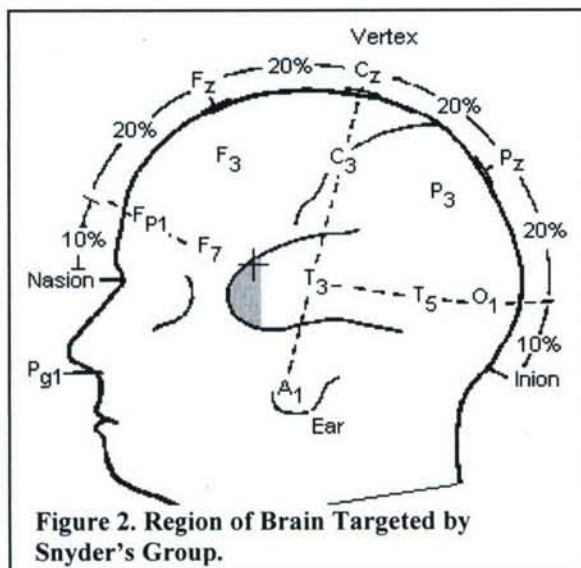
5.3 Savants and Paradoxical Functional Facilitation

Savants are individuals with exceptional skills within specific domains, such as drawing, memory, arithmetic, calendar calculations, and music. Most often, but not always, savant syndrome is found in individuals with autism. And, unfortunately, savants typically are not able to explain how they perform their feats. Recent studies have helped elucidate the neural mechanisms involved in savant abilities. As stated by Boff (2006), the challenge for human factors researchers becomes “how to effectively exploit this understanding to enhance the cognitive abilities of normal individuals”.

Many hypotheses have been developed concerning how savants acquire their peculiar skills. Some researchers suggest it is accomplished through repetitive practice, eidetic imagery, or high-speed calculation. However, this does not fit well with most reported cases of savants, as savant skills often suddenly materialize at an early age and are not improved by practice (O'Connor, 1989). Also, adult onset savant skills often occur suddenly following an accident or at the onset of fronto-temporal dementia (Snyder et al., 2003). To explain savant syndrome, Snyder and Mitchell (1999) proposed a theory referred to as “privileged access”. Because savant syndrome is often associated with some form of left-brain dysfunction, which is tied to hypothesis formation by searching for patterns and matching them to prior experience (Wolford et al., 2000), Snyder and colleagues (1999) have hypothesized that savants have access to lower level, more literal information. Another key component to savant skills is the lack of true creativity and an increased interest in details of faces, objects, shapes, and sounds. This lends further support to the theory that the fronto-temporal region of the brain is responsible for imposing experiences onto sensory information, as creativity is often considered to be a synthesis of experiences (Miller et al., 1998; Miller et al., 2000).

Snyder's group has based their approach heavily on the work of a neurologist at the University of California San Francisco, Dr. Bruce Miller. According to several accounts documented by Dr. Miller and others, adults can suddenly display savant

abilities late in life as a result of fronto-temporal lobe dementia or after head trauma to the region (Miller et al., 1998; Miller et al., 2000; Hou et al., 2000). It is also interesting to note that fronto-temporal lobe dementia has been characterized by an increase in slow-wave EEG activity (Lindau et al., 2003). The concept that has arisen from studies such as these is the idea of paradoxical functional facilitation (PFF), whereby direct or indirect neural damage may result in facilitation of behavioral functions. One of the best known examples of PFF is the Sprague effect, where collicular lesions may bring about an improvement in visual functioning following an initial occipital lesion (Sprague, 1991). Neurological hindrances can produce not only restoration of previously lost functions, but, in some cases, improvement above normal abilities in specific tasks (Kapur, 1996). It is hypothesized this results from a neuronal system being damaged or impaired that typically produces an inhibitory effect on some other functional system in the brain. Therefore, theoretically, it may be possible, using rTMS, to inhibit a region in the brain often seen damaged in individuals with savant abilities, allowing normal individuals an opportunity to access information in a PFF state.



To test their hypothesis, Dr. Snyder's group has applied rTMS to the left fronto-temporal lobe of normal subjects, inhibiting a part of the brain suspected to be involved with meaning and concepts, thereby allowing conscious access to literal details (Snyder et al., 2003; Snyder, Bahramali, Hawker, & Mitchell, 2006). Results from their studies have hinted at the possibility that this approach may work, as some subjects have shown improved abilities in numerosity (quickly surmising the number of objects briefly presented to them), proofreading, and stylized changes in drawing (Snyder et al., 2003; Snyder et

al., 2006) (for a personal review of Dr. Snyder's TMS work, see Attachment B). However, many brain stimulation experts, such as psychiatrist/neurologist Dr. Mark George of the Medical University of South Carolina, are still skeptical of the cognitive enhancing potential of TMS, especially using Snyder's savant abilities approach (M. George, personal communication, January 17, 2007).

5.4 Possible Methods to Improve Efficacy

Numerous variables can affect the efficacy of TMS. Research has demonstrated that the relative orientation of the neuron and the induced electrical field is important (Amassian, Quirk, & Stewart, 1990), as well as the polarity of the current in the coil (Sommer & Paulus, 2003). Further, it has been shown that the neural mechanism underlying cognitive enhancements might be frequency dependent. Working memory was shown to be facilitated with 5-Hz TMS, but not 1-Hz or 20-Hz (Luber et al., 2006). Even more so, the frequency dependence of enhancement effects might be dependent on natural brain rhythms. When individual alpha frequency rTMS was applied to mesial

frontal and right parietal sites prior to a mental rotation task, there was an increase in the amount of improvement versus control frequencies (Klimesch, Sauseng, & Gerloff, 2003).

Other possible methods that may potentiate stimulation-induced effects include pairing central nervous system and peripheral nervous system stimulation, combining multi-focal central nervous system stimulation to modulate circuit connectivity, and stimulation during task performance to entrain circuits or disrupt selective cognitive processes.

But perhaps the quickest way to improve the efficacy of TMS would be to combine it with functional imaging data. In Luber and colleagues' (submitted) article on improving performance after sleep deprivation with TMS, functional imaging data revealed specific neural networks affected by sleep deprivation, individualized for each subject. Stimulation was then applied to these tailored locations. While gross anatomical brain regions remain consistent brain-to-brain, the actual location of active neurons during processes may vary greatly. Thus, it is clear a TMS approach that incorporates imaging, tailored to the individual's neural circuitry is necessary. Another area that may benefit from functional imaging is the placement of the coil – its orientation relative to the sulci and gyri of the brain, neurons in the circuits, etc.

6. Other Methods for Enhancing Cognition

While the focus of this report is on the cognitive enhancing capabilities of TMS, there are other methods that also show promise. These range from brain stimulation methods somewhat similar to TMS to novel pharmacological agents.

Though TMS has many benefits, its limitations are apparent and "its adoption by the cognitive neuroscience community has been hindered by safety considerations, cost, and the awkwardness of the delivery system" (Wassermann & Grafman, 2005). As stated by Wassermann and Grafman (2005), "Particularly where the experimental or therapeutic goal is facilitation of brain processes, alternative means are needed." Transcranial direct current stimulation (tDCS) allows electrical polarization for modulating brain function. The main concept behind tDCS is that very weak currents passed through the human head can change the response of cerebral neurons and improve cognitive function. Sometimes, and perhaps more correctly, tDCS is referred to as transcranial direct current polarization.

With direct current stimulation, the brain is polarized with a 1-mA current by placing an active and inactive electrode on the head. The anodal stimulation is excitatory, facilitating the depolarization of neurons; cathodal stimulation is inhibitory. These effects last at least three minutes and can linger for hours. Furthermore, tDCS has been shown to modulate rTMS effects. Through tDCS, it may be possible to "prime" a region of the brain before TMS application, thereby enhancing the effect. Researchers demonstrated that tDCS sensitizes the cortex to neuroplastic effects of rTMS, achieving lasting after-effects (Lang et al., 2004).

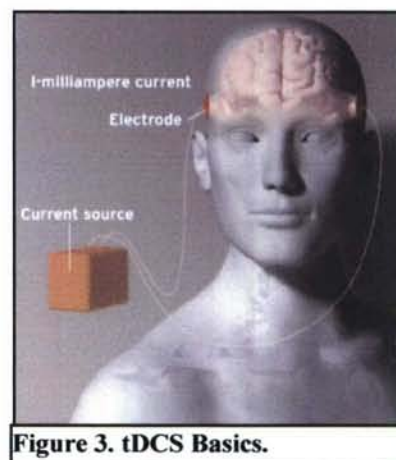


Figure 3. tDCS Basics.

But even on its own, evidence indicates that tDCS may have some potential to enhance cognitive abilities in normal individuals. Nitsche and colleagues (2003) reported improved initial learning tasks with anodal stimulation and improved skill in overlearned tasks with cathodal stimulation. A study by Kincses and colleagues (2004) indicated that implicit learning in a probabilistic classification paradigm could be improved by weak anodal tDCS over the prefrontal cortex, suggesting that increases in excitability in the area could have effects on learning and memory similar to the changes observed over the motor cortex. tDCS has even been shown to improve hand function in patients with chronic stroke (Hummel et al., 2005).

Though outside the scope of this report, it is also worth briefly mentioning recent advances in cognitive enhancing pharmacological agents. Some of the cognition-optimizing substances mentioned in the HPO final report (Russell, Bulkley, & Grafton, 2005) include ampakines and calcineurin inhibitors (optimizing neural connections), orexins (increase alertness and are involved in the sleep-wake cycle), and salvia lavandulaefolia (increase verbal recall). While these substances may provide benefits on their own accord, there may be an increased benefit when combined with brain stimulation technologies such as TMS or tDCS.

7. Conclusions and Recommendations

Based on my research for this project and the limited experience I have working for the Air Force Research Laboratory, I believe we should begin investing resources in this area of research. This is cutting edge technology with large possible pay-offs. Many academic TMS research facilities are still in their infancy, so they are not heavily rooted in clinical application research. It would be very easy to begin collaborative efforts with leading academia research teams to develop military applicable technologies and techniques. Not only does TMS offer new areas of research in enhancement of human effectiveness, but it also allows for improvements in existing legacy research, such as fatigue countermeasures, as demonstrated by the research group at Columbia University.

7.1 Possible Applications of Technology

To put it succinctly, some of the benefits TMS may offer include: facilitation of learning, memory, and information processing; remediation of performance following sleep deprivation; enhancing the restorative function of sleep through slow-wave oscillation induction; deception inhibition; treatment of post-traumatic stress disorder (PTSD) (Cohen et al., 2004); improved visual discrimination; and, improved vigilance abilities. Many of these enhancements could be of benefit to nearly every warfighter. With my background in unmanned aerial vehicles (UAVs), I can quickly see several possible applications in that realm. Sensor operators in UAV platforms with still and video imagery (e.g., Global Hawk and Predator, respectively) are the first group of operators I would target. In time, and with the input of others, I am confident the possible realm of applications for the Air Force will expand greatly.

7.2 Experts in Field for Future Collaborations

Leading the way in the optimization of TMS technology and paradigms is the group of researchers at Columbia University. Dr. Holly Lisanby and her colleague, Dr.

Bruce Luber, lead much of the brain stimulation work. Working in conjunction with them is Dr. Joy Hirsch, who leads the university's fMRI facility. Some of the issues currently being worked on by the group at Columbia include: where to stimulate (by mapping brain networks through TMS-fMRI equipment; constructing new coil designs for sleep, sham, and deep-brain stimulation); how to stimulate (pulse shape, frequency and pattern of pulse trains); and, when to stimulate (delivery relative to intrinsic brain activity with EEG-TMS synchronization).

Other prominent researchers in the area include Dr. Alvaro Pascual-Leone and his team at Harvard University. Their research tends to be more clinically-oriented, but this may overlap with Air Force interests as the augmentation of deficient cognitive abilities can have implications in the enhancement of normal individuals' abilities (or simply augmenting deficient ones due to fatigue, for example). Dr. Mark George and his group at the Medical University of South Carolina have led much of the work interleaving TMS with fMRI and attempting to construct a more portable TMS system. Dr. George has also recently released a book on clinical applications of TMS. At the National Institutes of Health, Dr. Eric Wassermann, chief of the Brain Stimulation Unit at the National Institute of Neurological Disorders and Stroke, has been pioneering much of the work with TMS and tDCS. He has created many of the safety guidelines now adhered to by the TMS research community.

This is by no means a comprehensive list of TMS researchers. These groups, however, seem to be pursuing TMS research most relevant to possible warfighter applications. Other groups, such as Dr. Ed Golob's lab at Tulane University, are beginning to conduct TMS research and also have interests in other areas relevant to the AF such as spatial audio. There are also international groups, such as Dr. Allan Snyder's Centre for the Mind at the University of Sydney, who are pursuing cognitive ability potentiation related research (see Attachment B).

7.3 Other Interested Agencies

Savant-like abilities have been suggested as being particularly well suited for detailed-oriented tasks such as fingerprint detection (L. Pring, personal communication, November 15, 2006). Besides this direct application, these abilities may transfer well to other tasks such as analyzing imagery, where technicians are required to discriminate between minuscule details. There may also be numerous applications of temporary inhibition (or excitation) of specific neural areas in the brain. For example, recent functional imaging research has revealed areas in the brain involved in deception (e.g., Langleben et al., 2002). With precise application of TMS, it may be possible to "turn off" a person's ability to deceive by inhibiting some of the neural circuits involved. Many Department of Defense and intelligence agencies (such as the CIA) may have an interest in this, as well as the Department of Justice. As more neural circuits are uncovered, more possibilities exist to facilitate or interrupt the neural transmission of those circuits – expanding the possible applications of technologies such as TMS.

Other less far-fetched possible interested agencies include AFOSR for some of the more basic scientific research that has yet to be done in this area, such as more fully understanding the underlying mechanisms at play during brain stimulation, the role (if any) of magnetite in the brain during TMS, etc. DARPA has already been investing in certain areas of TMS research, such as attempting to create a more portable unit and

using TMS to reduce the effects of fatigue. They may be interested in the imagery analyst application as they currently have a “Neurotechnology for Intelligence Analysts” program with the stated goal “to revolutionize the way that analysts handle intelligence imagery, increasing both the throughput of imagery to the analyst and overall accuracy of the assessments”. Columbia University is currently working on a white paper examining the effect of TMS on visual discriminability, which fits nicely into the goal of the DARPA program.

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Appendix A
Table with Studies of Slow rTMS Effects with
Normal Human Subjects (taken from Hoffman & Cavus, 2002)

Study	Site of Stimulation	Frequency (Hz)	Control/Comparison Stimulation Condition	Field Strength Relative to Motor Threshold (%)	Duration of Stimulation (minutes)	Number of Stimulation Sessions	Observed Effects
Chen et al. (8)	Left motor cortex	0.9	Prior stimulation trial at 0.1 Hz in same subjects	115	15	1	Decreased motor evoked potentials 15 minutes after rTMS
Wassermann et al. (9)	Left motor cortex	1	Sham stimulation	100	15	1	Decreased motor evoked potentials in contralateral motor cortex
Kimbrell et al. (10)	Right motor cortex	1	Half of subjects received sham stimulation only	110	30	1	Decreased glucose uptake relative to sham stimulation in motor cortex bilaterally, frontal cortex, and corpus striatum
Fox et al. (5)	Left motor cortex	1	Baseline scan before rTMS, three scans during rTMS, and two scans after rTMS	120	30	1	Increased blood flow in motor cortex and contralateral supplementary motor area, with decreased activation in contralateral motor cortex; direct effects lasted at least 10 minutes after rTMS
Bohning et al. (11)	Left motor cortex	1	None	80 and 110	— ^a	1	Increased blood-oxygen-level-dependent (BOLD) signal in ipsilateral motor cortex, with more signal at higher stimulation strength
Muellbacher et al. (12)	Right motor cortex	1	None	115	15	1	Decreased motor evoked potentials and increased motor threshold for 30 minutes after rTMS
Rossi et al. (13)	Left motor cortex	1	Sham stimulation	110	15	1	Decreased negative slope and duration of Bereitschaftspotential ^b
Maeda et al. (14)	Motor cortex	1	Stimulation at other frequencies (10 and 20 Hz)	90	4	2 ^c	Decreased motor evoked potentials on each of the 2 days of the study
Gerschlag et al. (15)	Left premotor cortex	1	rTMS of left prefrontal and parietal cortex	90	25	1	Decreased motor evoked potentials following rTMS of premotor cortex but not following rTMS of comparison regions
D'Alfonso et al. (16)	Left and right prefrontal cortex	0.6	Left- and right-sided stimulation compared	130	15	1 ^d	Right-sided stimulation reduced and left-sided stimulation increased avoidance reactions to threatening faces
Nahas et al. (17)	Left prefrontal cortex	1	Variable stimulation strengths	80, 100, and 120	— ^e	1	No activation of motor threshold with 80% strength, right prefrontal activation with 100%, bilateral prefrontal activation with 120%
Borojerdi et al. (18)	Visual cortex	1	Stimulation at another scalp location (Cz)	— ^f	15	1	Increased phosphene induction threshold for stimulation over visual cortex but not after control stimulation; increase lasted more than 10 minutes

^a Blocks of 18 pulses were interleaved with acquisition of BOLD signal.

^b A slow negative potential preceding motor actions that arises in the supplementary motor area of the frontal cortex.

^c One session per day.

^d One stimulation at each site on separate days.

^e Blocks of 21 pulses were interleaved with acquisition of BOLD signal.

^f The phosphene induction threshold was used as the measure of strength.

Appendix B

Trip Report to Centre for the Mind

Centre for the Mind (CFM)
University of Sydney
Sydney, New South Wales, Australia
March 12-16, 2007

Attendees:

1Lt Jeremy Nelson (USAF/AFRL)
Dr. Allan Snyder (CFM) and other CFM team members

Purpose:

The purpose of this trip was to visit the Centre for the Mind facilities at the University of Sydney (the Centre for the Mind also has facilities at the Australia National University in Canberra, Australia but they were not visited as part of this trip). During this visit the Centre's focus and planned research, as well as areas of overlapping research interests for both AFRL and the Centre were discussed.

Background:

The stated goal for the Centre for the Mind's research is to "understand what it means to be uniquely human and what it takes to be a champion." They approach this goal through the development of "technological ways to read the mind and artificial ways to enhance human creativity." My focus for the trip was on the Centre's work in enhancing cognitive abilities in normal subjects, but the Centre also does research in other areas with less direct warfighter applicability.

Of particular interest to the U.S. Air Force is the Centre's work with transcranial magnetic stimulation (TMS). A TMS machine consists of a coil of copper wire inside a paddle-shaped casing. Passing an electric current through the coil induces an intense magnetic field around it. By placing the coil on a person's scalp, the magnetic field penetrates about 2 cm into the person's skull, inducing an electric field in the brain tissue beneath. Depending on the strength of the field, the shape of the coil, and the rate of the electrical pulses (anywhere from a single pulse to 50 per second) this activates, slows down, or inhibits signaling in the targeted area of the brain.

Electrical stimulation to the brain is not a new concept, but the application of the stimulation has been refined greatly in the past few decades. With direct stimulation of the brain, all the neurons below the electrode are stimulated with a pulse (including pain-sensitive ones in the skin). TMS offers a focused, fairly noninvasive way to stimulate outer cortical brain regions without causing significant stimulation to the scalp. Since its introduction in the 1980s, TMS has

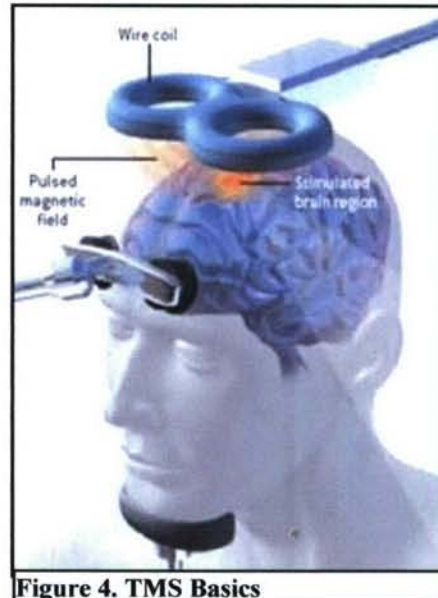


Figure 4. TMS Basics

been used successfully in studies to help alleviate depression, speed up reaction time, enhance reasoning abilities, and help improve cognitive performance after sleep deprivation. It is also worthy to note that some of this research has been sponsored by DARPA.

What makes the Centre for the Mind's research unique, besides the bold claims of turning normal individuals into "savants", is the theory upon which it is based. Experiments at the Centre are predicated on the idea that by inhibiting a region of the brain, a normal subject will gain "privileged access" to more literal sensory information. In this way, according to Dr. Snyder, normal individuals will temporarily behave like



Figure 5. Dr. Snyder (left) and the Centre's Experiment Station

savants. And unlike many other TMS researchers, Snyder's approach emphasizes the *inhibition* of a brain region whereas many researchers focus on *excitation*, such as "priming" a region of the brain by providing a small amount of stimulation before inducing activation of the area through the task. Snyder's main focus is on the visual system, although the Centre does have concurrent projects in the auditory domain.

Observations:

Dr. Snyder's theory about creating temporary savant-like abilities in normal people is ingenious and appealing. Could it really be as easy as turning off a part of the brain? There are several accounts of people with brain injuries or adult on-set dementia suddenly exhibiting amazing abilities, so it seems his theory is not unreasonable. Dr. Snyder's approach is based considerably on evidence by Dr. Bruce Miller, a neurologist at UC-San Francisco, who has studied savant-like transformations in patients with frontotemporal dementia.

While at the Centre, I was able to observe an experimental session following the methodologies described in the articles "Savant-like skills exposed in normal people by suppressing the left fronto-temporal lobe" (Snyder et al., 2003, *Journal of Integrative Neuroscience*, 2 (2), 149-158.) and "Savant-like numerosity skills revealed in normal people by magnetic pulse" (Synder et al., 2006, *Perception*, 35, 837-845.). I was also able to participate in the experiment as a subject; however, my prior knowledge of some of the measures being taken undoubtedly biased my results.

After being screened for participation, subjects are stimulated with single pulse TMS on their motor cortex to determine their individual motor threshold frequency. For the repetitive TMS portion of the experiment, subjects receive stimulation at 90% of this value. Subjects then sit in front of a computer screen and perform a baseline trial in each of the tasks - numerosity, proofreading, change blindness detection, word list recall, and drawing. For the numerosity task, subjects are presented a computer screen on which a random number of dots appear for 1.5 sec. The dots disappear and the subject is asked how many dots were on the screen. Although unknown to the subject, the number of dots generated varies randomly from 50 – 150. During the proofreading task, subjects are asked to read aloud proverbs that are shown on the screen. The proverbs are broken up so they appear like this:

“A bird in the
the hand is worth
two in the bush”

For the change blindness detection, subjects are shown a picture for about 1 sec and then an identical picture appears in the same location, except it contains a slight change from the previous picture. The original picture then appears again, and this continues for 20 changes (about 40 seconds) or until the subject locates and clicks on the changed region in the picture.



Figure 6. Change Blindness Example

In the word recall list, subjects are presented with a list of about 20 words at the rate of about one word per second, given an intervening task (in this case, one minute to draw a horse), and then shown a list of words one at a time and asked if each word was in the original list or not. The drawing task, which serves both as an intervening task for the word recall task and as a subjective look at the participant's drawing style, simply requires the subject to draw a specific animal within a time limit of one minute. Subjects then receive 15 minutes of repetitive TMS (1 pulse at 90% motor threshold value every second) at a site halfway between T3 and F7 on the 10-20 system for electrode placement, in the left anterior fronto-temporal region. Once the TMS session is complete, the subjects are run through the battery of tasks again.

In previously described methodologies (Snyder et al., 2003 & Snyder et al., 2006), TMS sham and post-TMS effect sessions were completed. However, these sessions were not performed during my visit. In the observed experiment, the subject showed slight improvement only in the numerosity task, which could be due to chance or practice effect.

Personal Experience:

While I admit a personal account of an experiment has limited scientific merit, it was perhaps the most important part of the trip for me. It is one thing to read about the application of a technology; it is another to experience it firsthand. Plus, who wouldn't want to be a savant for a day?

After Dr. Snyder recorded my motor threshold value, I started the experimental trials. Having read the above mentioned papers on Snyder's methodologies, I already knew the range of numbers used in the numerosity task, so my guesses were all within 50 to 150. Similarly, having previous knowledge of the proofreading task enabled me to

correctly detect all the errors. However, there was little way for me to have been prepared for the change blindness task or word recall task. I was able to detect the change in one of the three pictures presented. I also recalled all the words correctly and incorrectly identified two semantically similar words.

Once I had completed the first set of tasks (to include drawing a cat), I was then fitted with an EEG cap, and the midpoint between T3 and F7 location was marked on my head. With my chin resting on a stand, the TMS coil was aligned with the mark on my left frontotemporal region. The repetitive TMS pulse was delivered once a second for 15 minutes. Initially, the pulses caused a minor clenching of my jaw and twitching of the muscles around my left eye. According to Dr. Snyder and his team, this is common and most subjects tend to experience much more severe jaw clenching that persists throughout the 15 minutes. To help dampen this effect, subjects are usually provided a piece of gum. The TMS machine is loud and sounds (and, to some degree, feels) like a little hammer is beating the side of your head. It's a long 15 minutes.

After the time was up, I was put through the tasks a second time. My numerosity scores improved from 3 hits to 5 hits, but as mentioned earlier, my guesses had a greater chance of being accurate simply based on my knowledge of the defined range for the task. A hit is defined as a guess within $5 \pm$ the actual number of dots presented, and the task consisted of approximately 20 trials. An interesting note is that during my pre-TMS numerosity trials, the number that first came to mind was typically rounded to the nearest 5 or 10 (i.e., "135" or "90"), whereas in my post-TMS trials the first number that came to mind was not confined to this rounding (i.e., "113", "76", or "142"). This effect was also briefly discussed in Snyder's numerosity paper. I did not repeat the proofreading task as I had already found all the errors. Out of three change blindness pictures, I was able to detect an additional picture change, bringing my total to two out of the three pictures (I was presented with the same pictures as before the stimulation, which will be discussed in more detail below). Snyder and his team mentioned that I detected the most difficult picture, commonly missed by other subjects (with and without TMS). My word recall data had a computer error and so my performance was not recorded. However, I did perform it several minutes later after the error was brought to our attention. My performance had deteriorated as would be expected with an increased time delay memory recall task (I recalled correctly about 70% of the words and incorrectly identified several of the semantically similar words). My second drawing of a cat did not differ noticeably as a result of the TMS application.

It is difficult to say if I really noticed a difference while under the influence of repetitive TMS. I did have a strange, almost floating sensation, and I would like to think I was being more detail-oriented. At times, I felt like my eyes would immediately fixate on small, random details on the wall, on the ceiling, etc. However, I am hesitant to attribute this to the TMS because I could easily have been under a confirmation bias, finding evidence to fit my hopeful hypothesis. What I was hoping to see could easily have influenced what I was seeing.

Shortly after the experiment, I was led out into the quad area near the front of the school. We had arranged for me to come back the following morning for further discussion. On my way out, one of Dr. Snyder's team members commented on the architecture of the school and how it was modeled after Cambridge. Except, he said, it's the only school with a marsupial among the gargoyles. He said it was very difficult to

notice, but he'd walk me around front to get the best view and point it out. While we were still in the quad, I quickly glanced around and immediately found the kangaroo statue among the many gargoyles. At the next meeting, Snyder and his team thought it was very impressive that I was able to locate the kangaroo statue and attributed it to my TMS-induced abilities. I attribute it to my slight height advantage and natural tendency towards detail.

Conclusions:

Snyder's group has made bold claims about their results, yet they do admit to only about a 40% effectiveness rate. Neither my personal experience nor my observation of another subject who went through the experiment left me with the feeling that the current techniques can reliably produce "savant-like abilities in normal people". Some savant experts may agree with this low effectiveness rate, such as Dr. Darold Treffert, a Wisconsin psychiatrist, who has suggested that only some people have the neuronal architecture necessary for savant abilities. But I, along with Dr. Snyder's group, believe there are several factors that may increase the systematic efficacy of the technique.

In the application of TMS, there are many variables that can reduce the effectiveness of the magnetic pulses. One of the first discussions I had with Dr. Snyder was about the benefit of incorporating functional imaging into their experiments. In this way, the neural circuitry for each subject could first be mapped and the TMS could then be applied more precisely to the region dubbed "Miller's area", tailored specifically for each subject. Other factors that influence the effectiveness of TMS may include the orientation of the coil to the individual's brain structure (i.e., gyri folds), waveform of the pulse(s), individuals' endogenous brain rhythms, and thickness of the individual's hair and skull. Furthermore, nearly all studies with TMS are wrought with the difficulties of producing a realistic sham treatment. Due to certain aspects of TMS, many people can determine if they are receiving real or sham TMS. While the area of stimulation by TMS is fairly concentrated, the induced field is a graduated one, causing some stimulation of nerves between the coil and desired brain region. Because of this, subjects can often tell if they are not receiving TMS due to the lack of extraneous stimulation.

While the inhibition of a brain region is a central component of Dr. Snyder's theory, the brain is a complex organ with many different processes taking place at all times. To define an approach as solely excitative or inhibitive seems too limited. I would hypothesize an excite-*and*-inhibit approach where certain brain regions are inhibited while others are excited may be successful versus a dualistic excite-*or*-inhibit only approach. For example, the parietal cortex has been shown to be associated with numerosity estimation in brain imaging studies. By inhibiting "Miller's area" (as per Dr. Snyder's theory) as well as priming (i.e., exciting) the parietal area involved in numerosity, there may be a possibility for enhanced performance.

As for Snyder's current methodologies, I observed several areas where stricter experimental control may yield better results. With the actual testing, having the experimenter read a script would allow for consistent directions and procedures. At one point in my observations, there was a discussion about an explanation for a subject's performance. If standardized procedures and scripts were followed, it would ensure all subjects receive the exact same instructions. It also seems as though order effects may influence the results, and the effects reported would be strengthened if more experimental

control conditions were included (e.g., stimulating other areas of the brain to compare performance). I also noted that numerosity seems to be a skill that is highly susceptible to practice effects. Simply given more opportunities to guess will most likely lead to an increase in accuracy – other members on Snyder’s team seemed to agree that this appeared to be true. It also seemed that a different method of analyzing the numerosity data would perhaps yield more insightful results. Instead of simply giving a range and labeling “hit” or “miss”, a method that looks at all guesses and their relative distance from the correct number could possibly show trends towards greater accuracy.

Further, while the proofreading task is initially very interesting, once the trick is learned (the same word ends a line and repeats the start of the next line) the task becomes much less difficult on subsequent trials. Whether or not TMS allows a person to break away from their holistic processing of familiar stimuli to read what is actually on the screen versus what they know is, of course, the whole point of the task – but I am unsure if the current test is able to distinguish that. Perhaps a more basic Stroop reading task would suffice. Also, allowing subjects to read the same proverbs for all trials simply increases the number of opportunities he/she has to correctly identify the errors. For change blindness, it seems having more than 3 trials would allow for more statistically meaningful data. Also, using the same 3 picture scenes pre- and post-TMS simply allows more exposure to the scenes as the trials progress, hence more time to find the change in each scene. The word recall task seemed well constructed, except that tighter experimental controls would ensure consistent timing with the intervening task and recall task for all subjects since time delays have a definite effect on recall ability. The drawing task, while interesting, does not provide objective data and is subject to practice effects. Subjective analyses from this task should not be used as a basis for any conclusions, but perhaps as superfluous evidence to support main effects.

Next Step:

The next part of this project will consist of a visit by Dr. Snyder and, possibly, other members of his research team, to AFRL at Wright-Patterson AFB. During their visit, Dr. Snyder will deliver a lecture on his Centre’s current research efforts. Tours of AFRL facilities and discussions with other AFRL researchers will then take place to

begin constructing mutually beneficial research projects for AFRL and the Centre. In previous discussions with the Centre, we have briefly outlined studies investigating the ability of repetitive TMS to improve subjects’ abilities to discriminate fine detail on imagery (such as SAR) and to increase subjects’ vigilance by improving their ability to detect change while monitoring video feeds. I am also currently discussing possible collaborative research efforts in this area with TMS researchers at Columbia University.



Figure 7. SAR Imagery Example

List of Acronyms

AFOSR – Air Force Office of Scientific Research
AFRL – Air Force Research Laboratory
CFM – Centre for the Mind (University of Sydney, Australia)
DARPA – Defense Advanced Research Projects Agency
DC – Direct current
EEG – Electroencephalogram
fMRI – Functional magnetic resonance imaging
HE – Human Effectiveness Directorate
HPO – Human Performance Optimization
LIP – Left inferior parietal (lobule of the brain)
LTD – Long-term depression
LTP – Long-term potentiation
NIH – National Institute of Health
PET – Positron emission tomography
PFF – Paradoxical functional facilitation
PTSD – Post-traumatic stress disorder
rTMS – Repetitive transcranial magnetic stimulation
tDCS – Transcranial direct current stimulation
TMS – Transcranial magnetic stimulation
UAV – Unmanned aerial vehicle (or remotely piloted vehicle [RPV])
USAF – United States Air Force